

## EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	538	(560/174).CCLS.	USPAT; DERWENT	OR	OFF	2006/08/17 13:18
L2	4	((("6068991") or ("6395767"))).PN.	USPAT; DERWENT	OR	OFF	2006/08/17 13:20
L3	1	("11091183").PN.	USPAT; DERWENT	OR	OFF	2006/08/17 13:20
L4	147	(560/189).CCLS.	USPAT; DERWENT	OR	OFF	2006/08/17 13:21
L5	544	(560/155).CCLS.	USPAT; DERWENT	OR	OFF	2006/08/17 13:21
L6	758	(560/115).CCLS.	USPAT; DERWENT	OR	OFF	2006/08/17 13:22
L7	405	(560/226).CCLS.	USPAT; DERWENT	OR	OFF	2006/08/17 13:22

17/08/2006,10716012e.trn

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PASSWORD:

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SESSION RESUMED IN FILE 'HCAPLUS' AT 06:55:30 ON 17 AUG 2006  
FILE 'HCAPLUS' ENTERED AT 06:55:30 ON 17 AUG 2006  
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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	2.53	170.12

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	2.53	170.12

FILE 'REGISTRY' ENTERED AT 06:55:38 ON 17 AUG 2006  
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STRUCTURE FILE UPDATES: 16 AUG 2006 HIGHEST RN 902024-59-3  
DICTIONARY FILE UPDATES: 16 AUG 2006 HIGHEST RN 902024-59-3

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

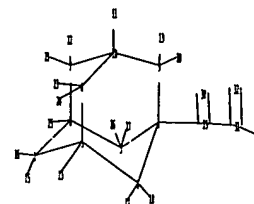
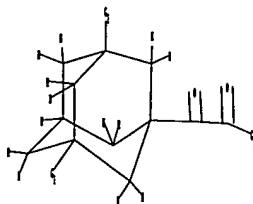
Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/ONLINE/UG/regprops.html>

=>

Uploading C:\Program Files\Stnexp\Queries\10716012e.str



chain nodes :  
 11 13 15 16 17 18 19 20 21 22 23 24 25 26 27 29 30 31 32 33  
 ring nodes :  
 1 2 3 4 5 6 7 8 9 10  
 chain bonds :  
 1-15 1-16 2-25 3-26 3-27 4-29 5-13 6-17 6-18 7-21 7-22 8-23 8-24 9-19  
 9-20 10-11 29-30 29-31 31-32 31-33  
 ring bonds :  
 1-2 1-5 2-3 2-7 3-4 4-6 4-9 5-6 5-8 7-10 8-10 9-10  
 exact/norm bonds :  
 1-2 1-5 2-3 2-7 3-4 4-6 4-9 5-6 5-8 5-13 7-10 8-10 9-10 10-11 29-30  
 31-32 31-33  
 exact bonds :  
 1-15 1-16 2-25 3-26 3-27 4-29 6-17 6-18 7-21 7-22 8-23 8-24 9-19 9-20  
 29-31

G1:OH,H

G2:O,NH2

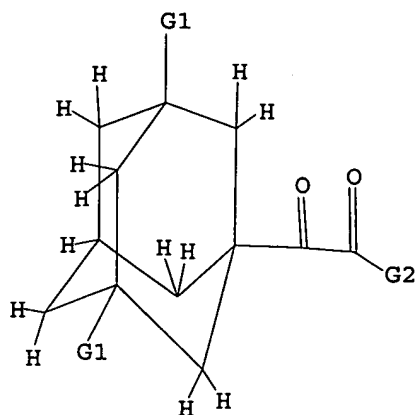
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 11:CLASS 13:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS 19:CLASS 20:CLASS  
 21:CLASS 22:CLASS 23:CLASS 24:CLASS 25:CLASS 26:CLASS 27:CLASS 29:CLASS  
 30:CLASS 31:CLASS 32:CLASS 33:CLASS

L5 STRUCTURE UPLOADED

=> d 15

L5 HAS NO ANSWERS

L5 STR



G1 OH,H

G2 O,NH2

Structure attributes must be viewed using STN Express query preparation.

=> s l5

SAMPLE SEARCH INITIATED 06:55:59 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 1562 TO ITERATE

100.0% PROCESSED 1562 ITERATIONS

1 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*

BATCH \*\*COMPLETE\*\*

PROJECTED ITERATIONS: 28870 TO 33610

PROJECTED ANSWERS: 1 TO 80

L6 1 SEA SSS SAM L5

=> s l5 full

FULL SEARCH INITIATED 06:56:04 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 31268 TO ITERATE

100.0% PROCESSED 31268 ITERATIONS

6 ANSWERS

SEARCH TIME: 00.00.01

L7 6 SEA SSS FUL L5

=> file hcaplus

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

166.94

337.06

FILE 'HCAPLUS' ENTERED AT 06:56:12 ON 17 AUG 2006

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FILE COVERS 1907 - 17 Aug 2006 VOL 145 ISS 8  
FILE LAST UPDATED: 16 Aug 2006 (20060816/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l7

L8 7 L7

=> d ed abs ibib hitstr 1-7

L8 ANSWER 1 OF 7 HCAPLUS COPYRIGHT 2006 ACS on STN

ED Entered STN: 24 Mar 2006

AB The title process comprises subjecting 1-acetyl-3-hydroxyadamantane to a liquid-phase oxidation with a permanganate salt (e.g., sodium permanganate) to produce 2-(3-hydroxy-1-adamantyl)-2-oxoacetic acid, or a salt, with acidification (e.g., hydrochloric acid) to form the free acid.

ACCESSION NUMBER: 2006:273089 HCAPLUS

DOCUMENT NUMBER: 144:311720

TITLE: Oxidative process for the preparation of 2-(3-hydroxy-1-adamantyl)-2-oxoacetic acid or its salts from 1-acetyl-3-hydroxyadamantane

INVENTOR(S): Williams, Eric L.

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 5 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

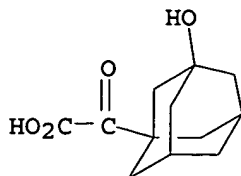
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006063950	A1	20060323	US 2005-228055	20050916
WO 2006034175	A1	20060330	WO 2005-US33446	20050916
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			

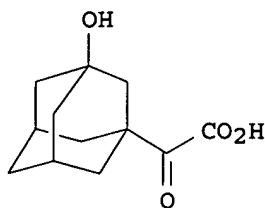
PRIORITY APPLN. INFO.: US 2004-610893P P 20040917

OTHER SOURCE(S): CASREACT 144:311720

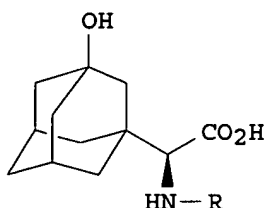
IT 709031-28-7P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (oxidative process for the preparation of 2-(3-hydroxy-1-adamantyl)-2-oxoacetic acid or its salts from 1-acetyl-3-hydroxyadamantane)  
 RN 709031-28-7 HCAPLUS  
 CN Tricyclo[3.3.1.1<sup>3,7</sup>]decane-1-acetic acid, 3-hydroxy- $\alpha$ -oxo- (9CI)  
 (CA INDEX NAME)



L8 ANSWER 2 OF 7 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ED Entered STN: 10 Nov 2005  
 GI



I



HN—R

II R=H

III R=BOC

AB A process for production of cyclopropyl-fused pyrrolidine-based inhibitors of dipeptidyl peptidase IV is provided which employs a BOC-protected amine of the structure (III) prepared by subjecting an acid of the structure (I) to reductive amination by treating the acid with ammonium formate, NAD, dithiothreitol and partially purified phenylalanine dehydrogenase/formate dehydrogenase enzyme concentrate (PDH/FDH) and without isolating treating the resulting amine of the structure (II) with di-tert-Bu dicarbonate to form the BOC-protected amine.

ACCESSION NUMBER: 2005:1192917 HCAPLUS  
 DOCUMENT NUMBER: 143:458679  
 TITLE: Chemoenzymic preparation of dipeptidyl IV inhibitors  
 INVENTOR(S): Politino, Michael; Cadin, Matthew M.; Skonezny, Paul M.; Chen, Jason G.  
 PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA  
 SOURCE: PCT Int. Appl., 73 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005106011	A2	20051110	WO 2005-US12615	20050413
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,				

GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ,  
LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA,  
NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL,  
SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA,  
ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,  
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,  
EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,  
RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,  
MR, NE, SN, TD, TG

US 2005260712

A1

20051124

US 2005-104015

20050412

PRIORITY APPLN. INFO.:

US 2004-561986P

P 20040414

OTHER SOURCE(S):

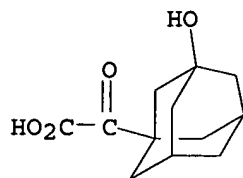
CASREACT 143:458679

IT 709031-28-7P

RL: BCP (Biochemical process); CPS (Chemical process); PEP (Physical,  
engineering or chemical process); PUR (Purification or recovery); RCT  
(Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP  
(Preparation); PROC (Process); RACT (Reactant or reagent)  
(chemoenzymic preparation of dipeptidyl IV inhibitors)

RN 709031-28-7 HCAPLUS

CN Tricyclo[3.3.1.1<sup>3,7</sup>]decane-1-acetic acid, 3-hydroxy- $\alpha$ -oxo- (9CI)  
(CA INDEX NAME)



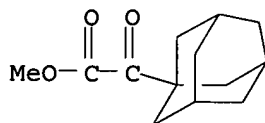
IT 709031-32-3P 709031-33-4P

RL: CPS (Chemical process); PEP (Physical, engineering or chemical  
process); PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic  
preparation); PREP (Preparation); PROC (Process); RACT (Reactant or  
reagent)

(chemoenzymic preparation of dipeptidyl IV inhibitors)

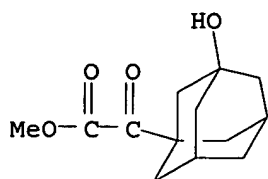
RN 709031-32-3 HCAPLUS

CN Tricyclo[3.3.1.1<sup>3,7</sup>]decane-1-acetic acid,  $\alpha$ -oxo-, methyl ester (9CI)  
(CA INDEX NAME)

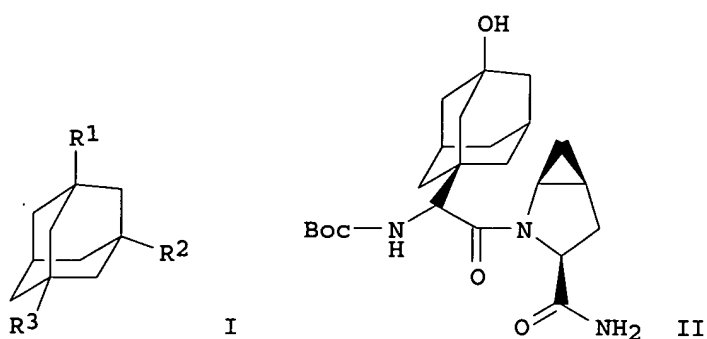


RN 709031-33-4 HCAPLUS

CN Tricyclo[3.3.1.1<sup>3,7</sup>]decane-1-acetic acid, 3-hydroxy- $\alpha$ -oxo-, methyl  
ester (9CI) (CA INDEX NAME)



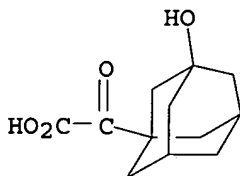
L8 ANSWER 3 OF 7 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ED Entered STN: 27 Jun 2004  
 GI



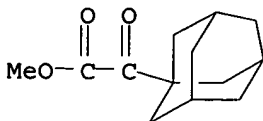
AB The invention provides methods and compds. for the production of cyclopropyl-fused pyrrolidine-based inhibitors of dipeptidyl peptidase IV. Also described are methods for the asym. reductive amination of (3-hydroxyadamantan-1-yl)oxoacetic acid. Adamantane derivs. I [R1 is H or OH; R2 is C(O)COR4, C(O)NR5R6, C(X)nCOR4 or C(NR7R8)COR4, where X is halo, n is 1-2, R4 is alkoxy, NH2 or OH, and R5-R8 are H or carbalkoxy; R3 is H, OH or NR9C(O)R10, where R9 is carboxy-substituted alkyl or aryl and R10 is 3-cyano-2-azabicyclo[3.1.0]hex-2-yl] or their pharmaceutically-acceptable salts are claimed. Thus, adamantyl-substituted glycineamide derivative II (Boc = tert-butoxycarbonyl) was prepared via amidation of Boc-protected (S)- $\alpha$ -amino-3-hydroxy-1-adamantaneacetic acid.

ACCESSION NUMBER: 2004:515478 HCAPLUS  
 DOCUMENT NUMBER: 141:54618  
 TITLE: Preparation of cyclopropyl-fused pyrrolidine-based inhibitors of dipeptidyl peptidase IV  
 INVENTOR(S): Vu, Truc Chi; Brzozowski, David B.; Fox, Rita; Godfrey, Jollie Duaine, Jr.; Hanson, Ronald L.; Kolotuchin, Sergei V.; Mazzullo, John A., Jr.; Patel, Ramesh N.; Wang, Jianji; Wong, Kwok; Yu, Jurong; Zhu, Jason; Magnin, David R.; Augeri, David J.; Hamann, Lawrence G.  
 PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA  
 SOURCE: PCT Int. Appl., 101 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

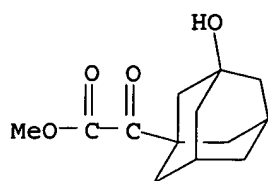
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004052850	A2	20040624	WO 2003-US38558	20031204
WO 2004052850	A3	20060302		
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US 2005090539	A1	20050428	US 2003-716012	20031118
CA 2508619	AA	20040624	CA 2003-2508619	20031204
AU 2003297647	A1	20040630	AU 2003-297647	20031204
EP 1581487	A2	20051005	EP 2003-812799	20031204
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003017139	A	20051129	BR 2003-17139	20031204
CN 1791401	A	20060621	CN 2003-80109631	20031204
JP 2006516121	T2	20060622	JP 2004-559282	20031204
PRIORITY APPLN. INFO.:			US 2002-431814P	P 20021209
			WO 2003-US38558	W 20031204
OTHER SOURCE(S): CASREACT 141:54618; MARPAT 141:54618				
IT 709031-28-7P 709031-32-3P 709031-33-4P				
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation of cyclopropyl-fused pyrrolidine-based inhibitors of dipeptidyl peptidase IV)				
RN 709031-28-7 HCAPLUS				
CN Tricyclo[3.3.1.1 <sup>3,7</sup> ]decane-1-acetic acid, 3-hydroxy- $\alpha$ -oxo- (9CI) (CA INDEX NAME)				



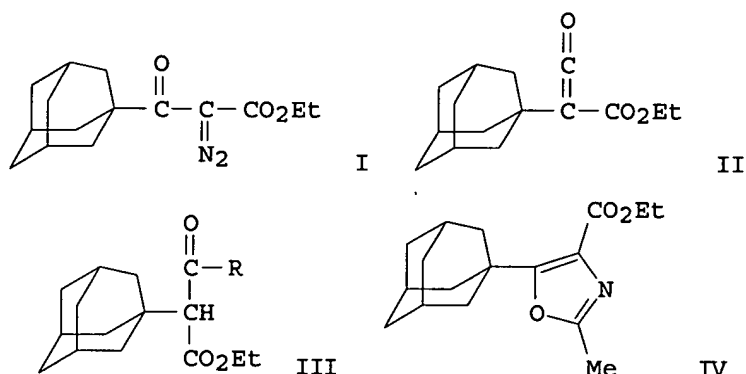
RN 709031-32-3 HCAPLUS  
 CN Tricyclo[3.3.1.1<sup>3,7</sup>]decane-1-acetic acid,  $\alpha$ -oxo-, methyl ester (9CI)  
 (CA INDEX NAME)



RN 709031-33-4 HCAPLUS  
 CN Tricyclo[3.3.1.1<sup>3,7</sup>]decane-1-acetic acid, 3-hydroxy- $\alpha$ -oxo-, methyl  
 ester (9CI) (CA INDEX NAME)



L8 ANSWER 4 OF 7 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ED Entered STN: 19 Feb 1994  
 GI



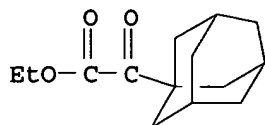
AB Title compound I was prepared by a diazo-transfer method, and cleanly converted to ketene II by photolysis, thermolysis or treatment with  $\text{Rh}(\text{OAc})_2$ . II was treated with  $\text{PhNH}_2$ , MeOH or  $\text{H}_2\text{O}$  to give diacid derivs. III ( $\text{R} = \text{PhNH}$ , OMe, OH), and gave a  $\beta$ -lactam on treatment with  $\text{PhCH:NPh}$ . Adamantyl heterocycles were also prepared from I; thus, treating I with MeCN in the presence of  $\text{BF}_3 \cdot \text{Et}_2\text{O}$  gave 76% oxazole IV. Fluorinating I with  $\text{BF}_3 \cdot \text{Et}_2\text{O}$  promoted dediazotization to give the corresponding  $\alpha$ -fluoro- $\beta$ -oxo ester.

ACCESSION NUMBER: 1994:76933 HCAPLUS  
 DOCUMENT NUMBER: 120:76933  
 TITLE: Ethyl 3-(1-adamantyl)-2-diazo-3-oxopropanoate:  
 synthetic use for the preparation of some adamantane  
 derivatives  
 AUTHOR(S): Ohno, Masatomi; Itoh, Motohiro; Ohashi, Toshiaki;  
 Eguchi, Shoji  
 CORPORATE SOURCE: Fac. Eng., Nagoya Univ., Nagoya, 464-01, Japan  
 SOURCE: Synthesis (1993), (8), 793-6  
 CODEN: SYNTBF; ISSN: 0039-7881  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 OTHER SOURCE(S): CASREACT 120:76933  
 IT 152240-45-4P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation and reactions of)

17/08/2006,10716012e.trn

RN 152240-45-4 HCAPLUS

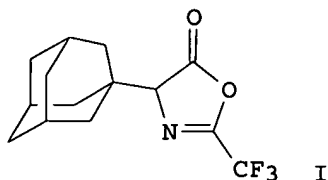
CN Tricyclo[3.3.1.1<sup>3,7</sup>]decane-1-acetic acid,  $\alpha$ -oxo-, ethyl ester (9CI)  
(CA INDEX NAME)



L8 ANSWER 5 OF 7 HCAPLUS COPYRIGHT 2006 ACS on STN

ED Entered STN: 05 Aug 1989

GI



AB Adamantyl-containing oxazolones, e.g., I, were prepared by treatment of adamantyl-containing amino acids or their N-acyl derivs. with water-removing agents. Thus, 2-(-1-adamantyl)glycine reacted with (CF<sub>3</sub>CO)<sub>2</sub>O in CF<sub>3</sub>CO<sub>2</sub>H to give 86% I. The conversion of the oxazolones to carboxylic acids amides was also described.

ACCESSION NUMBER: 1989:439230 HCAPLUS

DOCUMENT NUMBER: 111:39230

TITLE: Adamantyl-containing oxazolones and their derivatives

AUTHOR(S): Krasutskii, P. A.; Novikova, M. I.; Galina, T. P.

CORPORATE SOURCE: USSR

SOURCE: Vestnik Kievskogo Politekhnikeskogo Instituta,  
Khimicheskoe Mashinostroenie i Tekhnologiya (1988),  
25, 74-9

CODEN: VKMTAC; ISSN: 0372-6045

DOCUMENT TYPE: Journal

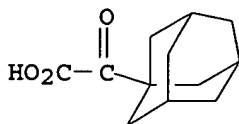
LANGUAGE: Russian

IT 16091-98-8P

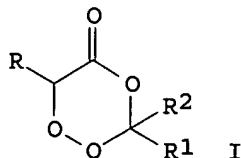
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of)

RN 16091-98-8 HCAPLUS

CN Tricyclo[3.3.1.1<sup>3,7</sup>]decane-1-acetic acid,  $\alpha$ -oxo- (9CI) (CA INDEX  
NAME)

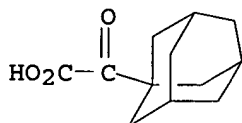


L8 ANSWER 6 OF 7 HCAPLUS COPYRIGHT 2006 ACS on STN  
ED Entered STN: 21 Aug 1987  
GI



AB 6-Monosubstituted 1,2,4-trioxan-5-ones I [R = 1-adamantyl, Me<sub>3</sub>C, Bu, n-hexyl; R<sub>1</sub> = R<sub>2</sub> = Me, R<sub>1</sub> = H, R<sub>2</sub> = Me, Me<sub>3</sub>C; R<sub>1</sub>R<sub>2</sub> = (CH<sub>2</sub>)<sub>5</sub>, 2-adamantylidene] undergo Et<sub>3</sub>N-catalyzed O-O bond cleavage to furnish 2-keto acids RCOC(=O)H in high yields, even when the R-substituents are bulky.

ACCESSION NUMBER: 1987:458139 HCAPLUS  
DOCUMENT NUMBER: 107:58139  
TITLE: Eliminative ring fission of 1,2,4-trioxan-5-ones. A new approach to  $\alpha$ -keto acids  
AUTHOR(S): Jefford, Charles W.; Rossier, Jean Claude; Boukouvalas, John  
CORPORATE SOURCE: Dep. Org. Chem., Univ. Geneva, Geneva, CH-1211, Switz.  
SOURCE: Journal of the Chemical Society, Chemical Communications (1986), (23), 1701-2  
CODEN: JCCCAT; ISSN: 0022-4936  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
OTHER SOURCE(S): CASREACT 107:58139  
IT 16091-98-8P  
RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of)  
RN 16091-98-8 HCAPLUS  
CN Tricyclo[3.3.1.1<sup>3,7</sup>]decane-1-acetic acid,  $\alpha$ -oxo- (9CI) (CA INDEX NAME)



L8 ANSWER 7 OF 7 HCAPLUS COPYRIGHT 2006 ACS on STN  
ED Entered STN: 12 May 1984  
GI For diagram(s), see printed CA Issue.  
AB Penicillins with general formula I (R = H or Me and X is H and an anion) were synthesized and exhibit excellent acid-sensitivity and resistance to penicillinase. Two general synthetic routes were used for preparation of I. In the first, the thiophenyl ester hydrochloride of an appropriate  $\alpha$ -amino-1-adamantaneacetic acid is treated with 6-aminopenicillanic acid in sodium or potassium hydrogen succinate buffer at 37°. After reaction, the mixture is acidified to pH 2 with HCl, and the thiophenol and succinic acid are removed by extraction with ether. The aqueous residue is adjusted to pH 4.6 with NaHCO<sub>3</sub> or KHCO<sub>3</sub> solution, and the solution

vacuum-concentrated at  $<35^{\circ}$  to give Na or K  $\alpha$ -amino- $\alpha$ -1-adamantylmethylpenicillin. The second route involves the reaction of the carboxylic anhydride of an appropriate  $\alpha$ -amino-1-adamantaneacetic acid with the Na or K salt of 6-aminopenicillanic acid in aqueous acetone at temps. between  $-15$  and  $50^{\circ}$ . The preparation of  $\alpha$ -amino-1-adamantaneacetic acids and their thiophenyl ester hydrochlorides and carboxylic anhydrides is discussed also. To prepare sodium  $\alpha$ -amino- $\alpha$ -methyl-1-adamantylmethylpenicillin (II), a mixture of 55 g.  $\text{NH}_4\text{Cl}$  and 62 g. 28%  $\text{NH}_4\text{OH}$  is added to a solution of 65 g. KCN in 240 ml.  $\text{H}_2\text{O}$ . A solution of 1 mole 1-adamantyl methyl ketone (Stetter and Rauscher, CA 55: 2517c; S. and Goebel, CA 57: 4560d) in 600 ml. EtOH is added, and the mixture heated at  $60^{\circ}$  for 5 hrs., cooled to  $0^{\circ}$ , and poured into 800 ml. cold concentrated HCl. This mixture is saturated with

HCl

gas, kept at  $5^{\circ}$  for 6 hrs., and diluted with 1000 ml.  $\text{H}_2\text{O}$ . The solution is refluxed for 3 hrs., cooled, decolorized with charcoal, and evaporated to dryness. The solids are triturated with Et<sub>2</sub>O and dissolved in  $\text{H}_2\text{O}$  and the aqueous solution is treated with a slight excess of  $\text{Ag}_2\text{CO}_3$ . The precipitate

of AgCl is

filtered and the filtrate made slightly acidic with HOAc and saturated with  $\text{H}_2\text{S}$ . The precipitate of  $\text{Ag}_2\text{S}$  is filtered, and the filtrate

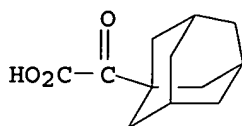
vacuum-concentrated to give

$\alpha$ -amino- $\alpha$ -methyl-1-adamantaneacetic acid (III). To prepare the thiophenyl ester hydrochloride (IV) of III, a suspension of 0.265 mole III in 1000 ml.  $\text{CH}_2\text{Cl}_2$  plus 4 ml. dimethyl formamide (DMF) is cooled to  $-5^{\circ}$ , and 80 g.  $\text{PCl}_5$  added. The mixts. is stirred for 15 min. at ice-bath temperature and 1 hr. at room temperature. The solid ( $\alpha$ -amino- $\alpha$ -methyl-1-adamantaneacetyl chloride, hydrochloride) is filtered and added to an ice-cold mixture of 100 ml. DMF and 44.1 g. thiophenol. The mixture is stirred at 1.5 hrs. and diluted with 1500 ml. ether to give IV. A mixture of 3.37 g. IV, 2.16 g. 6-aminopenicillanic acid, and 675 ml. 0.1M sodium hydrogen succinate is heated at  $37^{\circ}$  for 6 hrs., cooled to  $0^{\circ}$ , and adjusted to pH 2 with 1N HCl, and extracted with ether at  $0^{\circ}$ . The aqueous layer is adjusted to pH 4.65 with 3% aqueous  $\text{NaHCO}_3$ , and vacuum-concentrated at  $<35^{\circ}$  to give II. When 0.1M potassium hydrogen succinate is substituted for the 0.1M sodium hydrogen succinate, and when the pH is adjusted with aqueous  $\text{KHCO}_3$ , the product is potassium  $\alpha$ -amino- $\alpha$ -methyl-1-adamantylmethylpenicillin. When 1 mole 1-adamantanecarboxaldehyde (S. and R., CA 54: 18386b) is substituted for 1-adamantyl methyl ketone, sodium  $\alpha$ -amino-1-adamantylmethylpenicillin is obtained. Using the second route to prepare II, 1.88 g. 6-aminopenicillanic acid was suspended in 5 ml. water and 0.66 g.  $\text{NaHCO}_3$  was added slowly.  $\alpha$ -Amino-1-adamantaneacetic acid N-carboxylicanhydride (1.8 g.) was dissolved in 15 ml. acetone, and cooled to  $-25^{\circ}$  in a Dry Ice-acetone bath. The 6-aminopenicillanic acid- $\text{NaHCO}_3$ - $\text{H}_2\text{O}$  mixture was added, using 2.5 ml.  $\text{H}_2\text{O}$  to make the transfer, and the mixture stirred and kept at  $-15$  to  $-10^{\circ}$  for 15 min. and kept at room temperature 90 min. The solids were filtered and discarded. The filtrate was vacuum-evaporated, and the residue freeze-dried to yield 2.2 g. II, a light tan powder,  $245^{\circ}$  (decomposition). Similarly prepared were  $\alpha$ -amino-1-adamantaneacetic acid N-carboxylic anhydride;  $\alpha$ -amino-1-adamantaneacetic acid-HCl, m.  $320^{\circ}$  (decomposition); 1-adamantylglyoxylic acid oxime, m.  $174-6^{\circ}$ ; 1-adamantylglyoxylic acid, m.  $102-4^{\circ}$ ;  $\alpha$ -amino- $\alpha$ -methyl-1-adamantaneacetic acid N-carboxylic anhydride,  $\alpha$ -amino- $\alpha$ -methyl-1-adamantaneacetic acid-HCl, 5-adamantyl-5-methylhydantoin, m.  $330-40^{\circ}$  (decomposition). The penicillins showed activity against pneumococci, streptococci, and staphylococci. In addition, these compds. are useful in treatment of gram-neg. organisms and can be used against organisms usually resistant to non-synthetic penicillins.

17/08/2006,10716012e.trn

ACCESSION NUMBER: 1967:490798 HCAPLUS  
DOCUMENT NUMBER: 67:90798  
TITLE:  $\alpha$ -Amino-1-adamantylmethylpenicillins  
INVENTOR(S): Hermann, Edward C.; Snyder, Jack Austin  
PATENT ASSIGNEE(S): du Pont de Nemours, E. I., and Co.  
SOURCE: U.S., 3 pp.  
CODEN: USXXAM  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	----	-----	-----	-----
	US 3325478		19670713	US	19641117
IT	16091-98-8P				
	RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of)				
RN	16091-98-8 HCAPLUS				
CN	Tricyclo[3.3.1.1 <sup>3,7</sup> ]decane-1-acetic acid, $\alpha$ -oxo- (9CI) (CA INDEX NAME)				



=> log h

COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
43.36	380.42

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE	TOTAL
ENTRY	SESSION
-5.25	-5.25

CA SUBSCRIBER PRICE

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STN INTERNATIONAL SESSION SUSPENDED AT 06:57:49 ON 17 AUG 2006

17/08/2006,10716012g.trn

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PASSWORD:

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SESSION RESUMED IN FILE 'HCAPLUS' AT 07:36:56 ON 17 AUG 2006  
FILE 'HCAPLUS' ENTERED AT 07:36:56 ON 17 AUG 2006  
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COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	17.86	567.75
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
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CA SUBSCRIBER PRICE	-2.25	-7.50

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	ENTRY	SESSION
FULL ESTIMATED COST	22.92	572.81
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	ENTRY	SESSION
CA SUBSCRIBER PRICE	-2.25	-7.50

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DICTIONARY FILE UPDATES: 16 AUG 2006 HIGHEST RN 902024-59-3

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TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

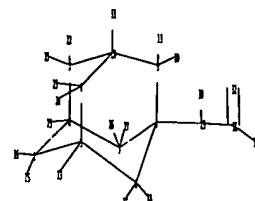
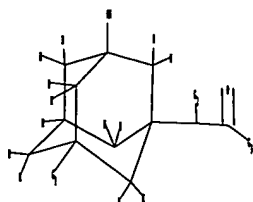
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chain nodes :  
 11 13 15 16 17 18 19 20 21 22 23 24 25 26 27 29 30 31 32 33 35  
 ring nodes :  
 1 2 3 4 5 6 7 8 9 10  
 chain bonds :  
 1-15 1-16 2-25 3-26 3-27 4-29 5-13 6-17 6-18 7-21 7-22 8-23 8-24 9-19  
 9-20 10-11 29-30 29-31 31-32 31-33  
 ring bonds :  
 1-2 1-5 2-3 2-7 3-4 4-6 4-9 5-6 5-8 7-10 8-10 9-10  
 exact/norm bonds :  
 1-2 1-5 2-3 2-7 3-4 4-6 4-9 5-6 5-8 5-13 7-10 8-10 9-10 10-11 29-30  
 31-32 31-33  
 exact bonds :  
 1-15 1-16 2-25 3-26 3-27 4-29 6-17 6-18 7-21 7-22 8-23 8-24 9-19 9-20  
 29-31

G1:OH,H

G2:NH2,NH

G3:OH,O

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom  
 11:CLASS 13:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS 19:CLASS 20:CLASS  
 21:CLASS 22:CLASS 23:CLASS 24:CLASS 25:CLASS 26:CLASS 27:CLASS 29:CLASS  
 30:CLASS 31:CLASS 32:CLASS 33:CLASS 35:CLASS

17/08/2006,10716012g.trn

L13        STRUCTURE UPLOADED

=> d l13

L13 HAS NO ANSWERS

L13        STR

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

Structure attributes must be viewed using STN Express query preparation.

=> s l13

SAMPLE SEARCH INITIATED 07:38:54 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED -        9 TO ITERATE

100.0% PROCESSED        9 ITERATIONS

0 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:    ONLINE    \*\*COMPLETE\*\*

BATCH    \*\*COMPLETE\*\*

PROJECTED ITERATIONS:        9 TO        360

PROJECTED ANSWERS:        0 TO        0

L14        0 SEA SSS SAM L13

=> s l13 full

FULL SEARCH INITIATED 07:38:59 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED -        156 TO ITERATE

100.0% PROCESSED        156 ITERATIONS

5 ANSWERS

SEARCH TIME: 00.00.01

L15        5 SEA SSS FUL L13

=> file hcaplus

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

167.38

740.19

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

TOTAL

ENTRY

SESSION

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-7.50

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FILE COVERS 1907 - 17 Aug 2006 VOL 145 ISS 8

Young, Shawquia, Page 3

17/08/2006,10716012g.trn

FILE LAST UPDATED: 16 Aug 2006 (20060816/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.

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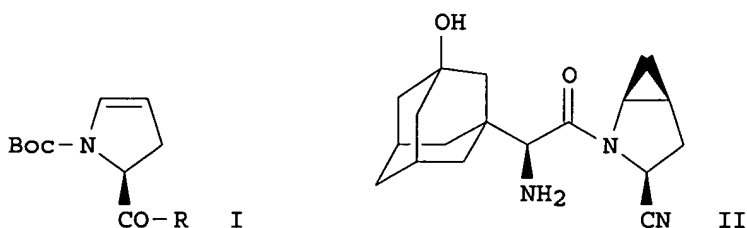
L16 12 L15

=> d ed abs ibib hitstr 1-12

L16 ANSWER 1 OF 12 HCAPLUS COPYRIGHT 2006 ACS on STN

ED Entered STN: 17 Feb 2006

GI



AB The invention describes a process for preparing pyrrolinecarboxamide intermediate I (R = NH<sub>2</sub>, Boc = tert-butoxycarbonyl) used in the synthesis of dipeptidyl peptidase IV (DPP IV) inhibitor II. Thus, a solution of crude I (R = OEt) in methanol containing NaOMe and formamide was stirred for 3.5 h at room temperature and the reaction mixture diluted by addition of saturated aqueous ammonium chloride followed by toluene and water; workup afforded I (R = NH<sub>2</sub>). The product was converted into II by cyclopropanation, coupling with Boc-protected (αS)-α-amino-3-hydroxytricyclo[3.3.1.1.3]decane-1-acetic acid, and deprotection reactions.

ACCESSION NUMBER: 2006:149261 HCAPLUS

DOCUMENT NUMBER: 144:192509

TITLE: Ammonolysis process for the preparation of intermediates for pyrrolidine-based dipeptidyl peptidase IV inhibitors

INVENTOR(S): Sharma, Padam N.; Galvin, Gabriel M.; Boettger, Susan D.; Racha, Saibaba; Zhu, Jingyang; Melton, Jack; Mudryk, Boguslaw M.

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 11 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

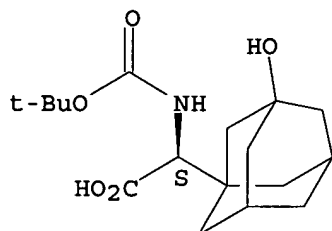
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006035954	A1	20060216	US 2005-199539	20050808
WO 2006020664	A2	20060223	WO 2005-US28310	20050810
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,				

GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ,  
 LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA,  
 NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK,  
 SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU,  
 ZA, ZM, ZW  
 RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,  
 IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,  
 CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,  
 GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,  
 KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2004-600510P P 20040811  
 OTHER SOURCE(S): CASREACT 144:192509; MARPAT 144:192509

IT 361442-00-4P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (ammonolysis of pyrrolinecarboxylate in preparation of intermediates for  
 pyrrolidine-based dipeptidyl peptidase IV inhibitors)  
 RN 361442-00-4 HCAPLUS  
 CN Tricyclo[3.3.1.1<sup>3,7</sup>]decane-1-acetic acid,  $\alpha$ -[[[(1,1-  
 dimethylethoxy)carbonyl]amino]-3-hydroxy-, ( $\alpha$ S)- (9CI) (CA INDEX  
 NAME)

Absolute stereochemistry.

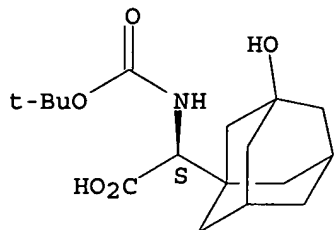


L16 ANSWER 2 OF 12 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ED Entered STN: 12 Feb 2006  
 AB A series of seco-prolinenitrile-containing dipeptides were synthesized and  
 assayed as inhibitors of the N-terminal sequence-specific serine protease  
 dipeptidyl peptidase IV, a promising new target for treatment of type 2  
 diabetes. The inhibitors described herein assess the min. structural  
 requirements at P1 for this enzyme, resulting in the identification of  
 inhibitors with low nM potency.  
 ACCESSION NUMBER: 2006:128531 HCAPLUS  
 DOCUMENT NUMBER: 144:370409  
 TITLE: Seco-prolinenitrile inhibitors of dipeptidyl peptidase  
 IV define minimal pharmacophore requirements at P1  
 AUTHOR(S): Magnin, David R.; Taunk, Prakash C.; Robertson, James  
 G.; Wang, Aiyang; Marcinkeviciene, Jovita; Kirby, Mark  
 S.; Hamann, Lawrence G.  
 CORPORATE SOURCE: Department of Discovery Chemistry, Bristol-Myers  
 Squibb, Pharmaceutical Research Institute, Princeton,  
 NJ, 08543-5400, USA  
 SOURCE: Bioorganic & Medicinal Chemistry Letters (2006),  
 16(6), 1731-1734  
 CODEN: BMCLE8; ISSN: 0960-894X  
 PUBLISHER: Elsevier B.V.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 OTHER SOURCE(S): CASREACT 144:370409

17/08/2006,10716012g.trn

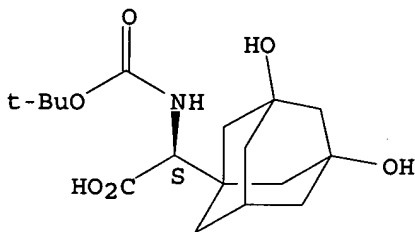
IT 361442-00-4 681282-72-4  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(synthesis and structure-activity relationship of seco-prolinenitrile-  
containing dipeptides, inhibitors of dipeptidyl peptidase IV for treatment  
of type 2 diabetes)  
RN 361442-00-4 HCAPLUS  
CN Tricyclo[3.3.1.1<sup>3,7</sup>]decane-1-acetic acid,  $\alpha$ -[[[(1,1-  
dimethylethoxy)carbonyl]amino]-3-hydroxy-, ( $\alpha$ S)- (9CI) (CA INDEX  
NAME)

Absolute stereochemistry.



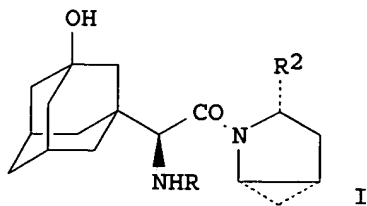
RN 681282-72-4 HCAPLUS  
CN Tricyclo[3.3.1.1<sup>3,7</sup>]decane-1-acetic acid,  $\alpha$ -[[[(1,1-  
dimethylethoxy)carbonyl]amino]-3,5-dihydroxy-, ( $\alpha$ S)- (9CI) (CA  
INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 3 OF 12 HCAPLUS COPYRIGHT 2006 ACS on STN  
ED Entered STN: 02 Dec 2005  
GI



AB A process was provided for preparing the dipeptidyl peptidase IV inhibitor

saxagliptin I (R = H, R<sub>2</sub> = CN) by a one-pot direct dehydration of amide I (R = CO<sub>2</sub>CMe<sub>3</sub>, R<sub>2</sub> = CONH<sub>2</sub>) using phosphorus oxychloride in an organic solvent, such as dichloromethane, quenching the reaction mixture with water to form the hydrochloric acid salt of I (R = H, R<sub>2</sub> = CN) and treating the salt with a base, such as NaOH, to form I.

ACCESSION NUMBER: 2005:1265198 HCAPLUS  
 DOCUMENT NUMBER: 144:23129  
 TITLE: Process for producing a dipeptidyl peptidase IV inhibitor  
 INVENTOR(S): Sharma, Padam N.  
 PATENT ASSIGNEE(S): USA  
 SOURCE: U.S. Pat. Appl. Publ., 8 pp.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

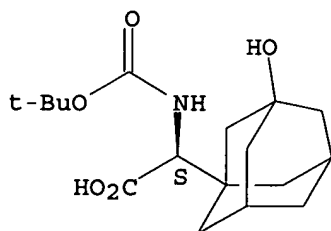
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005267191	A1	20051201	US 2005-135217	20050523
WO 2005115982	A1	20051208	WO 2005-US18205	20050524

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2004-574177P P 20040525  
 OTHER SOURCE(S): CASREACT 144:23129  
 IT 361442-00-4P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (process for the preparation of saxagliptin, a dipeptidyl peptidase IV inhibitor, via a one-pot dehydration using phosphorus oxychloride)  
 RN 361442-00-4 HCAPLUS  
 CN Tricyclo[3.3.1.1<sup>3,7</sup>]decane-1-acetic acid,  $\alpha$ -[[[(1,1-dimethylethoxy)carbonyl]amino]-3-hydroxy-, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



17/08/2006,10716012g.trn

ED Entered STN: 18 Nov 2005

AB An enzymic ammonolysis process is provided for the preparation of intermediates used in preparing dipeptidyl peptidase IV inhibitors wherein the enzyme *Candida antarctica* lipase-B is used to catalyze the ammonolysis process.

ACCESSION NUMBER: 2005:1224408 HCAPLUS

DOCUMENT NUMBER: 143:458687

TITLE: Enzymatic ammonolysis process for the preparation of intermediates for DPP IV inhibitors

INVENTOR(S): Patel, Ramesh N.; Hanson, Ronald L.; Gill, Iqbal; Brzozowski, David B.; Skonezny, Paul M.; Politino, Michael; Chen, Jason G.; Moris-Varas, Francisco; White, Brenda J.

PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA

SOURCE: PCT Int. Appl., 33 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

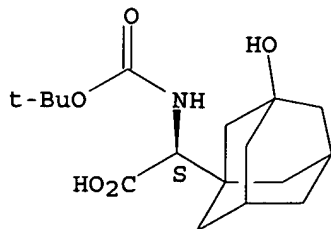
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

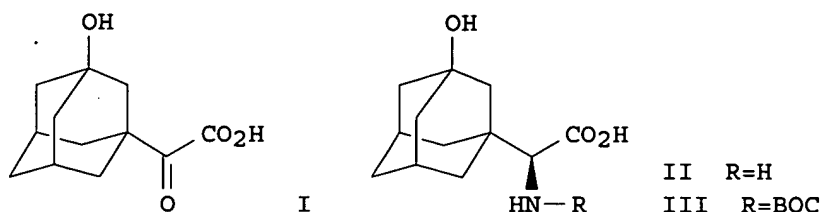
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005108594	A1	20051117	WO 2005-US15199	20050503
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005256019	A1	20051117	US 2005-119552	20050502
PRIORITY APPLN. INFO.:			US 2004-568097P	P 20040504
OTHER SOURCE(S):	MARPAT 143:458687			
IT 361442-00-4P				
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)				
(enzymic ammonolysis process for the preparation of intermediates for dipeptidyl peptidase IV inhibitors)				
RN 361442-00-4	HCAPLUS			
CN	Tricyclo[3.3.1.1 <sup>3,7</sup> ]decane-1-acetic acid, $\alpha$ -[[[(1,1-dimethylethoxy)carbonyl]amino]-3-hydroxy-, ( $\alpha$ S)- (9CI) (CA INDEX NAME)			

Absolute stereochemistry.



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 5 OF 12 HCAPLUS COPYRIGHT 2006 ACS on STN  
ED Entered STN: 10 Nov 2005  
GI



AB A process for production of cyclopropyl-fused pyrrolidine-based inhibitors of dipeptidyl peptidase IV is provided which employs a BOC-protected amine of the structure (III) prepared by subjecting an acid of the structure (I) to reductive amination by treating the acid with ammonium formate, NAD, dithiothreitol and partially purified phenylalanine dehydrogenase/formate dehydrogenase enzyme concentrate (PDH/FDH) and without isolating treating the resulting amine of the structure (II) with di-tert-Bu dicarbonate to form the BOC-protected amine.

ACCESSION NUMBER: 2005:1192917 HCAPLUS  
DOCUMENT NUMBER: 143:458679  
TITLE: Chemoenzymic preparation of dipeptidyl IV inhibitors  
INVENTOR(S): Politino, Michael; Cadin, Matthew M.; Skonezny, Paul M.; Chen, Jason G.  
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA  
SOURCE: PCT Int. Appl., 73 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005106011	A2	20051110	WO 2005-US12615	20050413
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005260712	A1	20051124	US 2005-104015	20050412
PRIORITY APPLN. INFO.:			US 2004-561986P	P 20040414
OTHER SOURCE(S):	CASREACT 143:458679			
IT 361442-00-4P				

17/08/2006,10716012g.trn

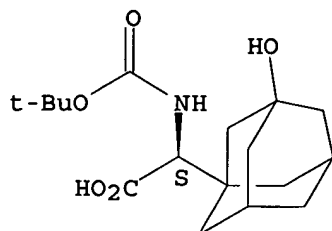
RL: CPS (Chemical process); PEP (Physical, engineering or chemical process); PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); PROC (Process); RACT (Reactant or reagent)

(chemoenzymic preparation of dipeptidyl IV inhibitors)

RN 361442-00-4 HCAPLUS

CN Tricyclo[3.3.1.1<sup>3,7</sup>]decane-1-acetic acid,  $\alpha$ -[[[(1,1-dimethylethoxy)carbonyl]amino]-3-hydroxy-, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

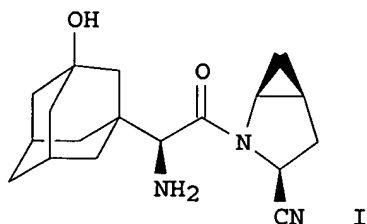
Absolute stereochemistry.



L16 ANSWER 6 OF 12 HCAPLUS COPYRIGHT 2006 ACS on STN

ED Entered STN: 07 Oct 2005

GI



AB Dipeptidyl peptidase IV inhibitor I was prepared by amidation of cyclopropyl-fused pyrrolidinecarbonitrile with (hydroxyadamantyl)aminoacetyl chloride N,O-bis(trifluoroacetyl) derivative and deprotection.

ACCESSION NUMBER: 2005:1078267 HCAPLUS

DOCUMENT NUMBER: 143:347457

TITLE: Process for preparation of cyclopropyl-fused pyrrolidine-based inhibitor of dipeptidyl peptidase IV

INVENTOR(S): Sharma, Padam N.; Gublo, Edward J.; Galvin, Gabriel

M.; Boettger, Susan D.; Racha, Saibaba

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 18 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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US 2005222242      A1      20051006      US 2005-91183      20050328
WO 2005094323      A2      20051013      WO 2005-US10424    20050329
W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
    CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
    GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
    LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
    NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM,
    SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW:  BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
    AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
    EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,
    RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
    MR, NE, SN, TD, TG

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PRIORITY APPLN. INFO.:

US 2004-558014P

P 20040331

OTHER SOURCE(S):

CASREACT 143:347457

IT 859202-35-0P

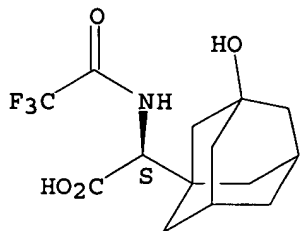
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)

(preparation of cyclopropyl-fused pyrrolidine-based inhibitor of dipeptidyl  
peptidase IV)

RN 859202-35-0 HCAPLUS

CN Tricyclo[3.3.1.1<sup>3,7</sup>]decane-1-acetic acid, 3-hydroxy- $\alpha$ -  
[(trifluoroacetyl)amino]-, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L16 ANSWER 7 OF 12 HCAPLUS COPYRIGHT 2006 ACS on STN

ED Entered STN: 22 Jul 2005

AB C3-19 alkyl and aryl thiotrifluoroacetates (e.g., 1-dodecyl thiotrifluoroacetate), which are prepared by the esterification of alkyl or aryl thiols with trifluoroacetic anhydride in the presence of an organic base (e.g., pyridine), a solvent (e.g., dichloromethane), and 4-(dimethylamino)pyridine as an esterification catalyst, are useful trifluoroacetyl protecting agents for the amino or hydroxy functional groups of amines, amino acids or primary or secondary alcs. or amino alcs. to enable formation of amide bonds in peptides or proteins which are useful as screening agents, pharmaceuticals, and cosmetics. A process is also described, using the title thiol esters, for protecting a primary or secondary amino group or a primary or secondary hydroxyl group or an amino alc. with a trifluoroacetyl protecting group in basic aqueous solution

ACCESSION NUMBER: 2005:641946 HCAPLUS

DOCUMENT NUMBER: 143:133093

TITLE: Process for the preparation of alkyl and aryl  
thiotrifluoroacetates useful as a source of  
trifluoroacetyl blocking groups for amines and amino  
acids

INVENTOR(S): Sharma, Padam N.; Gublo, Edward J.; Boettger, Susan  
D.; Racha, Saibaba; Usher, John

PATENT ASSIGNEE(S): USA  
 SOURCE: U.S. Pat. Appl. Publ., 7 pp.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005159612	A1	20050721	US 2005-32734	20050111
WO 2005073185	A1	20050811	WO 2005-US1012	20050112

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW  
 RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2004-537832P P 20040121

OTHER SOURCE(S): CASREACT 143:133093; MARPAT 143:133093

IT 859202-35-0P

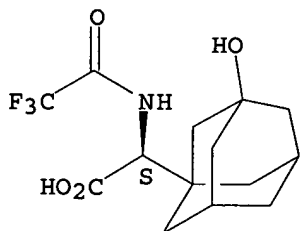
RL: SPN (Synthetic preparation); PREP (Preparation)

(process for the preparation of alkyl and aryl thiotrifluoroacetates useful as a source of trifluoroacetyl blocking groups for amines and amino acids)

RN 859202-35-0 HCAPLUS

CN Tricyclo[3.3.1.1<sup>3,7</sup>]decane-1-acetic acid, 3-hydroxy- $\alpha$ -[(trifluoroacetyl)amino]-, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L16 ANSWER 8 OF 12 HCAPLUS COPYRIGHT 2006 ACS on STN

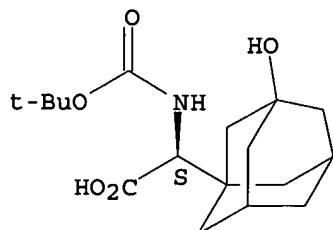
ED Entered STN: 24 Jun 2005

AB Efforts to further elucidate structure-activity relationships (SAR) within the authors previously disclosed series of  $\beta$ -quaternary amino acid linked L-cis-4,5-methanoproline nitrile dipeptidyl peptidase IV (DPP-IV) inhibitors led to the investigation of vinyl substitution at the  $\beta$ -position of  $\alpha$ -cycloalkyl-substituted glycines. Despite poor systemic exposure, vinyl-substituted compds. showed extended duration of action in acute rat ex vivo plasma DPP-IV inhibition models. Oxygenated putative metabolites were prepared and were shown to exhibit the potency and extended duration of action of their precursors in efficacy models measuring glucose clearance in Zuckerfa/fa rats. Extension of this approach to adamantylglycine-derived inhibitors led to the discovery of

highly potent inhibitors, including hydroxyadamantyl compound BMS-477118 (saxagliptin), a highly efficacious, stable, and long-acting DPP-IV inhibitor, which is currently undergoing clin. trials for treatment of type 2 diabetes.

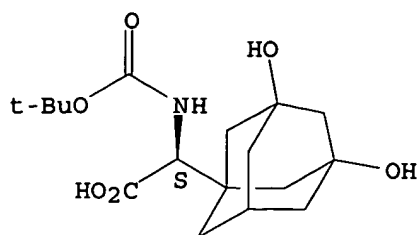
ACCESSION NUMBER: 2005:543673 HCAPLUS  
DOCUMENT NUMBER: 143:221803  
TITLE: Discovery and Preclinical Profile of Saxagliptin (BMS-477118): A Highly Potent, Long-Acting, Orally Active Dipeptidyl Peptidase IV Inhibitor for the Treatment of Type 2 Diabetes  
AUTHOR(S): Augeri, David J.; Robl, Jeffrey A.; Betebenner, David A.; Magnin, David R.; Khanna, Ashish; Robertson, James G.; Wang, Aiyang; Simpkins, Ligaya M.; Taunk, Prakash; Huang, Qi; Han, Song-Ping; Abboa-Offei, Benoni; Cap, Michael; Xin, Li; Tao, Li; Tozzo, Effie; Welzel, Gustav E.; Egan, Donald M.; Marcinkeviciene, Jovita; Chang, Shu Y.; Biller, Scott A.; Kirby, Mark S.; Parker, Rex A.; Hamann, Lawrence G.  
CORPORATE SOURCE: Department of Discovery Chemistry, Bristol-Myers Squibb, Princeton, NJ, 08543-5400, USA  
SOURCE: Journal of Medicinal Chemistry (2005), 48(15), 5025-5037  
CODEN: JMCMAR; ISSN: 0022-2623  
PUBLISHER: American Chemical Society  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
IT 361442-00-4P 681282-72-4P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(discovery and preclin. profile of saxagliptin (BMS-477118) as highly potent and long-acting and orally active dipeptidyl peptidase IV inhibitor for treatment of type 2 diabetes)  
RN 361442-00-4 HCAPLUS  
CN Tricyclo[3.3.1.1<sup>3,7</sup>]decane-1-acetic acid,  $\alpha$ -[[[(1,1-dimethylethoxy)carbonyl]amino]-3-hydroxy-, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



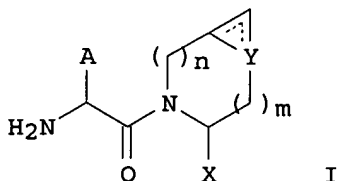
RN 681282-72-4 HCAPLUS  
CN Tricyclo[3.3.1.1<sup>3,7</sup>]decane-1-acetic acid,  $\alpha$ -[[[(1,1-dimethylethoxy)carbonyl]amino]-3,5-dihydroxy-, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 9 OF 12 HCAPLUS COPYRIGHT 2006 ACS on STN  
ED Entered STN: 11 Feb 2005  
GI



AB Title compds. [I; m, n = 0-2; m+n ≤2; dashed bonds form a cyclopropyl ring when Y = CH; X = H, CN; Y = CH, CH2, CHF, CF2, O, S, SO, SO2; A = (substituted) adamantyl], were prepared Thus, (S)-(3-hydroxy-5,7-dimethyladamantan-1-yl)glycine pyrrolidinamide (preparation from 3,5-dimethyladamantane-1-carboxylic acid given) at 3 μmol/kg orally in rats gave a 39% reduction in serum glucose after 4 h.

ACCESSION NUMBER: 2005:120884 HCAPLUS  
DOCUMENT NUMBER: 142:219555  
TITLE: Preparation of adamantylglycinamide inhibitors of dipeptidyl peptidase IV  
INVENTOR(S): Hamann, Lawrence G.; Khanna, Ashish; Kirby, Mark S.; Magnin, David R.; Simpkins, Ligaya M.; Sutton, James C.; Robl, Jeffrey  
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA  
SOURCE: PCT Int. Appl., 69 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005012249	A2	20050210	WO 2004-US24257	20040728
WO 2005012249	A3	20050506		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,

17/08/2006,10716012g.trn

NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,  
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW  
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,  
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,  
EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,  
SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,  
SN, TD, TG

US 2005038020 A1 20050217 US 2004-899641 20040727

US 6995183 B2 20060207

EP 1658066 A2 20060524 EP 2004-779352 20040728

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR

US 2005228021 A1 20051013 US 2005-149414 20050609

US 2005239839 A1 20051027 US 2005-149408 20050609

PRIORITY APPLN. INFO.:

US 2003-491832P P 20030801

US 2004-899641 A 20040727

WO 2004-US24257 W 20040728

OTHER SOURCE(S): MARPAT 142:219555

IT 361442-00-4P 681282-72-4P

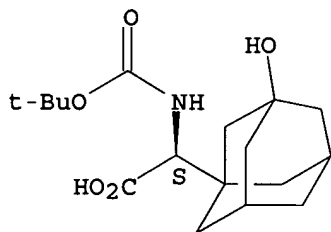
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)

(preparation of adamantylglycinamide inhibitors of dipeptidyl peptidase IV)

RN 361442-00-4 HCAPLUS

CN Tricyclo[3.3.1.1<sup>3,7</sup>]decane-1-acetic acid,  $\alpha$ -[[[(1,1-  
dimethylethoxy)carbonyl]amino]-3-hydroxy-, ( $\alpha$ S)- (9CI) (CA INDEX  
NAME)

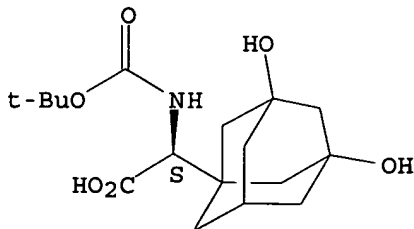
Absolute stereochemistry.



RN 681282-72-4 HCAPLUS

CN Tricyclo[3.3.1.1<sup>3,7</sup>]decane-1-acetic acid,  $\alpha$ -[[[(1,1-  
dimethylethoxy)carbonyl]amino]-3,5-dihydroxy-, ( $\alpha$ S)- (9CI) (CA  
INDEX NAME)

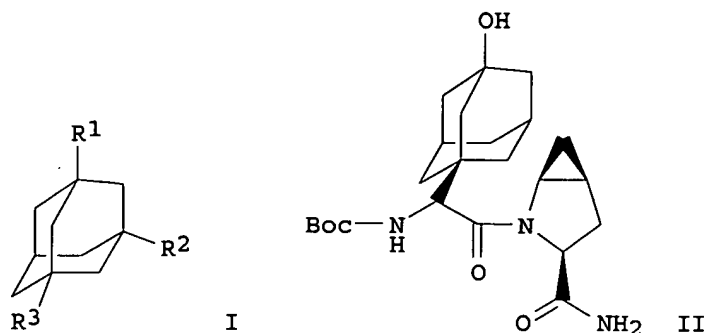
Absolute stereochemistry.



L16 ANSWER 10 OF 12 HCAPLUS COPYRIGHT 2006 ACS on STN

ED Entered STN: 27 Jun 2004

GI



AB The invention provides methods and compds. for the production of cyclopropyl-fused pyrrolidine-based inhibitors of dipeptidyl peptidase IV. Also described are methods for the asym. reductive amination of (3-hydroxyadamantan-1-yl)oxoacetic acid. Adamantane derivs. I [R<sup>1</sup> is H or OH; R<sup>2</sup> is C(O)COR<sup>4</sup>, C(O)NR<sup>5</sup>R<sup>6</sup>, C(X)<sub>n</sub>COR<sup>4</sup> or C(NR<sup>7</sup>R<sup>8</sup>)COR<sup>4</sup>, where X is halo, n is 1-2, R<sup>4</sup> is alkoxy, NH<sub>2</sub> or OH, and R<sup>5</sup>-R<sup>8</sup> are H or carbalkoxy; R<sup>3</sup> is H, OH or NR<sup>9</sup>C(O)R<sup>10</sup>, where R<sup>9</sup> is carboxy-substituted alkyl or aryl and R<sup>10</sup> is 3-cyano-2-azabicyclo[3.1.0]hex-2-yl] or their pharmaceutically-acceptable salts are claimed. Thus, adamantyl-substituted glycine derivative II (Boc = tert-butoxycarbonyl) was prepared via amidation of Boc-protected (S)-α-amino-3-hydroxy-1-adamantaneacetic acid.

ACCESSION NUMBER: 2004:515478 HCAPLUS

DOCUMENT NUMBER: 141:54618

TITLE: Preparation of cyclopropyl-fused pyrrolidine-based inhibitors of dipeptidyl peptidase IV

INVENTOR(S): Vu, Truc Chi; Brzozowski, David B.; Fox, Rita; Godfrey, Jollie Duaine, Jr.; Hanson, Ronald L.; Kolotuchin, Sergei V.; Mazzullo, John A., Jr.; Patel, Ramesh N.; Wang, Jianji; Wong, Kwok; Yu, Jurong; Zhu, Jason; Magnin, David R.; Augeri, David J.; Hamann, Lawrence G.

PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA

SOURCE: PCT Int. Appl., 101 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004052850	A2	20040624	WO 2003-US38558	20031204
WO 2004052850	A3	20060302		
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CA 2508619	AA	20040624	CA 2003-2508619	20031204
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EP 1581487	A2	20051005	EP 2003-812799	20031204

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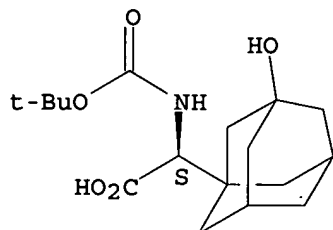
PRIORITY APPLN. INFO.: US 2002-431814P P 20021209  
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OTHER SOURCE(S): CASREACT 141:54618; MARPAT 141:54618

IT 361442-00-4P  
 RL: BPN (Biosynthetic preparation); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)  
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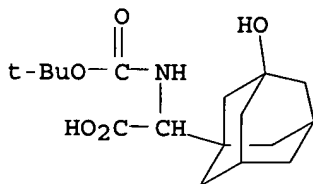
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Absolute stereochemistry.



IT 709031-31-2P 709031-42-5P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation of cyclopropyl-fused pyrrolidine-based inhibitors of dipeptidyl peptidase IV)

RN 709031-31-2 HCAPLUS  
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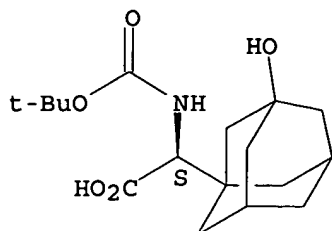
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CM 1

CRN 361442-00-4

CMF C17 H27 N O5

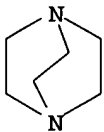
Absolute stereochemistry.



CM 2

CRN 280-57-9

CMF C6 H12 N2



L16 ANSWER 11 OF 12 HCAPLUS COPYRIGHT 2006 ACS on STN

ED Entered STN: 06 May 2004

AB Glycinenitrile derivs. R4NHCHR3CONR2CHR1CN [R1 is H, alk(en)(yn)yl or (cyclo)alk(en)yl; R2 is (un)substituted alk(en)(yn)yl, (cyclo)alk(en)yl or arylalk(en)(yn)yl; R3 is group given for R2 or cycloalkylalkyl, alkylthioalkyl, arylalkylthioalkyl, (hetero)aryl, heteroarylalkyl, cycloheteroalkyl or cycloheteroalkylalkyl, which may be substituted; R4 is H or can combine with R3 to form a 4- to 5-membered heterocyclic ring] were prepared for use in pharmaceutical compns. for the treatment of diabetes and related diseases. Thus, (S)-H2NCH(Ad)CONEtCH2CN was prepared by condensation of (S)-Boc-NHCH(Ad)CO2H (Boc = tert-butoxycarbonyl) with EtNHCH2CN (syntheses given), followed by deprotection using trifluoroacetic acid.

ACCESSION NUMBER: 2004:368874 HCAPLUS

DOCUMENT NUMBER: 140:357672

TITLE: Preparation of glycinenitrile-based inhibitors of dipeptidyl peptidase IV

INVENTOR(S): Magnin, David R.; Hamann, Lawrence G.

PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA

SOURCE: PCT Int. Appl., 57 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.

KIND

DATE

APPLICATION NO.

DATE

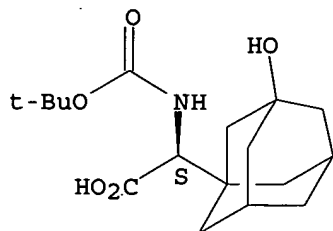
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    OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
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AU 2003282983      A1      20040513      AU 2003-282983      20031021
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EP 1553937          A2      20050720      EP 2003-774915      20031021
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PRIORITY APPLN. INFO.:      US 2002-420603P      P 20021023
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OTHER SOURCE(S):      MARPAT 140:357672
IT  361442-00-4P 681282-72-4P
RL:  RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
    (Reactant or reagent)
    (preparation of glycinenitrile amino acid derivs. as inhibitors of
    dipeptidyl peptidase IV)
RN  361442-00-4 HCAPLUS
CN  Tricyclo[3.3.1.13,7]decane-1-acetic acid,  $\alpha$ -[[[(1,1-
    dimethylethoxy)carbonyl]amino]-3-hydroxy-, ( $\alpha$ S)- (9CI) (CA INDEX
    NAME)

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Absolute stereochemistry.

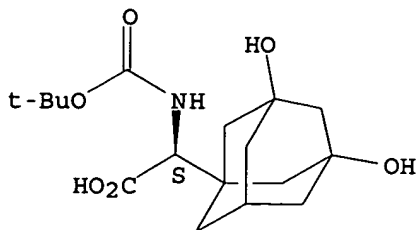


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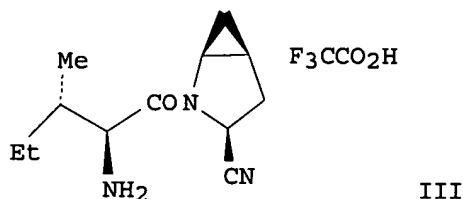
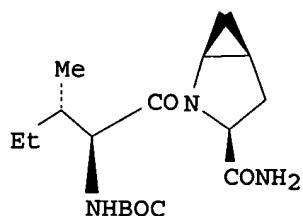
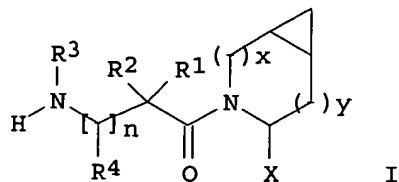
RN  681282-72-4 HCAPLUS
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    dimethylethoxy)carbonyl]amino]-3,5-dihydroxy-, ( $\alpha$ S)- (9CI) (CA
    INDEX NAME)

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Absolute stereochemistry.



L16 ANSWER 12 OF 12 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ED Entered STN: 21 Sep 2001  
 GI



AB Dipeptidyl peptidase IV inhibiting compds. I ( $x = 0$  or  $1$  and  $y = 0$  or  $1$  provided that  $x = 1$  when  $y = 0$  and  $x = 0$  when  $y = 1$ ;  $n = 0, 1$ ;  $X = H, CN$ ;  $R_1, R_2, R_3$  and  $R_4$  = same or different and independently selected from  $H$ , (un)substituted chain or cyclic components) and the pharmaceutically acceptable salts or prodrugs (no data) were prepared. Thus L-pyroglutamic acid Et ester was protected, cyclopropanated and reacted further with (S)-N-BOC-isoleucine providing an intermediate II which reacted further to yield the fused cyclopropylpyrrolidine III in 57% yield. A method is also provided for treating diabetes and related diseases, especially Type II diabetes, and other diseases by employing a title DP 4 inhibitor or a combination of DP 4 inhibitor and one or more of another antidiabetic agent such as metformin, glyburide, troglitazone, pioglitazone, rosiglitazone and/or insulin and/or one or more of a hypolipidemic agent and/or anti-obesity agent and/or other therapeutic agent.

ACCESSION NUMBER: 2001:693281 HCAPLUS

DOCUMENT NUMBER: 135:257147

TITLE: Preparation of fused cyclopropylpyrrolidine-based inhibitors of dipeptidyl peptidase IV

INVENTOR(S): Robl, Jeffrey A.; Sulsky, Richard B.; Augeri, David J.; Magnin, David R.; Hamann, Lawrence G.; Betebenner, David A.

PATENT ASSIGNEE(S): Bristol-Myers Squibb Co., USA

SOURCE: PCT Int. Appl., 135 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

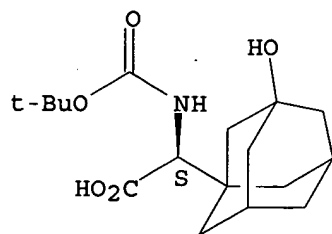
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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17/08/2006,10716012g.trn

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WO 2001068603 A3 20020214  
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US 2002019411 A1 20020214 US 2001-788173 20010216  
US 6395767 B2 20020528  
CA 2402894 AA 20010920 CA 2001-2402894 20010305  
EP 1261586 A2 20021204 EP 2001-918383 20010305  
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JP 2003531118 T2 20031021 JP 2001-567699 20010305  
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ZA 2002006816 A 20031126 ZA 2002-6816 20020826  
NO 2002004295 A 20021106 NO 2002-4295 20020909  
PRIORITY APPLN. INFO.:  
US 2000-188555P P 20000310  
CN 2001-806315 A3 20010305  
EP 2001-918383 A3 20010305  
WO 2001-US7151 W 20010305  
OTHER SOURCE(S): MARPAT 135:257147  
IT 361442-00-4P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(preparation of fused cyclopropylpyrrolidine-based inhibitors of dipeptidyl  
peptidase IV)  
RN 361442-00-4 HCAPLUS  
CN Tricyclo[3.3.1.1<sup>3,7</sup>]decane-1-acetic acid,  $\alpha$ -[[[(1,1-  
dimethylethoxy)carbonyl]amino]-3-hydroxy-, ( $\alpha$ S)- (9CI) (CA INDEX  
NAME)

Absolute stereochemistry.



=> log h

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

66.38

806.57

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

TOTAL